IN THE SPECIFICATION:

Please replace the 5th paragraph, lines 12-15, page 5, with the following:

~~Fig. 7 is a graph showing~~ Fig. 7 and Fig. 8 (left panel) are results showing in Example 6 that a GFP-rat Nox1 fusion polypeptide is produced, that the coexpression of RNAi(1), RNAi(3), and RNAi(5) inhibits the production of a GFP-rat Nox1 fusion protein dose-dependently ~~on their vectors (left panel)~~ on each vector (Fig. 7), and that the RNAi constructs have high specificity to their target gene ~~(right panel)~~ (Fig. 8 left panel);

Please replace the 6th paragraph, lines 16-18, page 5, with the following:

~~Fig. 8~~ Fig. 8 (right panel) is an electrophoretic image obtained in Example 6 by conducting RT-PCR to confirm that the mRNA expression of endogenous Nox1 is inhibited in each of cells, as compared to K-Ras-NRK and K-Ras-NRK/neg-1 cells;

Please replace the 9th paragraph, lines 25-26, page 5, with the following:

Fig. 11 is a graph showing the influence of reactivation of Nox1 once inhibited by siRNA on cells in terms of cell growth rates in Example 7;

Please replace the 10th paragraph, lines 27-30, page 5, with the following:

Fig. 12 is a graph showing a result of investigating adhesion-dependent cell growth capacity by use of a soft agar culture method in order to examine the influence of reactivation of Nox1 once inhibited by siRNA on cells by observing anchorage-independent growth capacity in Example 7;

Please replace the 11th paragraph, lines 31-33, page 5, with the following:

Fig. 13 is a ~~graph~~ photograph showing a result of observing morphological changes in cells in order to investigate the influence of Nox1 gene expression on transformation with mutant Ras in ~~Example 9~~ Example 8; and

Please replace the 1st paragraph, lines 3-15, page 12, with the following:

The pharmaceutical composition comprising the antibody of the present invention can be administered to, for example, humans or other mammals (e.g., rats, mice, guinea

pigs, rabbits, sheep, pigs, cattle, horses, cats, dogs, and monkeys). The amount of the pharmaceutical composition administered appropriately differs depending on the condition of objects to be administered, administration routes, and so on. For example, when orally administered, the pharmaceutical composition is generally administered at approximately 10 to 4000 mg, preferably approximately 20 to 2000 mg, more preferably approximately 50 to 500 mg, per day for an adult patient weighing 60 kg. When parenterally administered, it is preferred that the ~~siRNA~~ composition, for example in the form of injection, should be administered through the vein at a dose of approximately 10 to 2000 mg, preferably approximately 20 to 1000 mg, more preferably approximately 50 to 500 mg, per day for an adult patient weighing 60 kg although the dose differs depending on objects to be administered, the condition of ~~liver~~ target cancer, and so on.

Please replace the 2nd full paragraph, lines 12-16, page 14, with the following:

In the present invention, ~~siRNA or~~ siRNA corresponding to a polynucleotide comprising the nucleotide sequence of SEQ ID NO: 1 or a fragment thereof suppresses Nox1 gene expression and reduces Nox1 polypeptide production. Thus, the use of the siRNA or oligonucleotide will allow the inhibition of cell carcinogenesis or cancer progression induced by a mutant Ras gene.

Please replace the 4th paragraph, lines 20-23, page 14, with the following:

The siRNA of the present invention may correspond to a polynucleotide comprising a nucleotide sequence at positions from 71 to 1615 of SEQ ID NO: 1 or a fragment thereof. The length of the siRNA is less than 100 bp and is preferably 8 to 99 bp, particularly preferably 10 to 30 bp. Moreover, preferable examples of the ~~ssi~~ siRNA include the followings:

Please replace the 1st full paragraph, lines 3-6, page 15, with the following:

The siRNA of the present invention can be used by directly administrating the siRNA to a patient to be treated; by ~~infecting~~ transfecting the siRNA into a cell taken out of a patient to be treated and then returning the cell to the patient; or by administering an

expression vector incorporating the siRNA therein to a patient to be treated and expressing the siRNA.

Please replace the last paragraph, line 24, page 20 through line 2, page 21, with the following:

Three clones of the cell lines stably transfected with each of the RNAi(1), RNAi(3), and RNAi(5) (K-Ras-NRK/RNAi(1)-7, K-Ras-NRK/RNAi(1)-12, and K-Ras-NRK/RNAi(1)-15; K-Ras-NRK/RNAi(3)-17, K-Ras-NRK/RNAi(3)-19, and K-Ras-NRK/RNAi(3)-96; and K-Ras-NRK/RNAi(5)-2, K-Ras-NRK/RNAi(5)-3, and K-Ras-NRK/RNAi(5)-7) as well as two clones of the cells stably transfected with the pSilencer hygro Negative Control plasmid (K-Ras-NRK/neg-1 and K-Ras-NRK/~~neg-2~~ neg 3) were selected. The transfection of these constructions was confirmed by PCR using M13F and 3.0Rev as primers (Fig. 2). PCR temperature conditions were set to 94°C for 2 minutes, 30 cycles of (94°C for 1 minute, 60°C for 1 minute, and 72°C for 1 minute), followed by 72°C for 10 minutes. A thermal cycler used was Takara Thermal Cycler SP (Takara Shuzo Company Limited).

Please replace the 2nd paragraph, lines 11-23, page 21, with the following:

Subsequently, soft agar culture assay was performed in order to examine the transformation of the cells by observing anchorage-independent growth capacity. An agarose layer containing 0.53% agar and nutrients necessary for cell growth was placed and solidified in a culture dish of 6 cm in diameter, on which the cells suspended in a DMEM containing 0.3% agar and 10% FBS were then piled up at a final concentration of $1.5x10^4$ cells/culture dish. Subsequently, the cells were cultured at 37°C under a 5% CO_2 moisture environment to observe the appearance of cell colonies over 3 weeks. The adhesion-dependent cell growth of the cell lines exhibited by the soft agar culture was measured, and +/- average standard deviation (s.e.m.) from three measurements was shown in Fig. 4. As a result, the formation of many colonies was observed in the K-Ras-NRK cells and the transfected cells with the pSilencer hygro Negative Control plasmid (neg-1 and ~~neg-2~~ neg-3), whereas colony formation was remarkably inhibited in the transfection with the RNAi(1) to RNAi(5).

Please replace the last paragraph, line 21, page 22 through line 2, page 23, with the following:

The present inventors conducted analysis in the following procedures in order to confirm Nox1 expression decreased by the RNAi(1), RNAi(3), and RNAi(5): GFP-rat Nox1 was subjected to cotransfection with each of the RNAi(1) to (5) and subsequently immunoblotting analysis was conducted in the same way as in Example 2 in order to evaluate the inhibitory effect of the RNAi(1), RNAi(3), and RNAi(5) on GFP-rat Nox1 expression. As shown in ~~the left panel of~~ Fig. 7, it was revealed that an expected GFP-rat Nox1 fusion polypeptide is produced, and that the coexpression of the RNAi(1), RNAi(3), and RNAi(5) suppresses the production of a GFP-rat Nox1 fusion protein dependently on a dose of these vectors. GFP-Nox1 expression shown in ~~the left panel of~~ Fig. 7 was quantitatively determined by immunoblotting using an anti-GFP antibody. Numerals in ~~the left panel of~~ Fig. 7 denote the amount (μg) of DNA transfected. Both RNAi(1) and RNAi(5) are targeted for rat Nox1. The same approach as in ~~the left panel of~~ Fig. 7 was used to show in the ~~right panel of Fig. 7~~ left panel of Fig. 8 that the RNAi(1) and RNAi(5) do not inhibit human Nox1, that is, the RNAi constructions have high specificity to their target gene.

Please replace the 1st paragraph, lines 3-7, page 23, with the following:

Moreover, RT-PCR demonstrated that the mRNA expression of endogenous Nox1 is certainly inhibited in each of the K-Ras-NRK/RNAi(1)-7, K-Ras-NRK/RNAi(1)-12, K-Ras-NRK/RNAi(3)-19, K-Ras-NRK/RNAi(3)-96, K-Ras-NRK/RNAi(5)-2, K-Ras-NRK/RNAi(5)-7 cells, as compared to the K-Ras-NRK and K-Ras-NRK/neg-1 cells. The result is shown in the left panel of Fig. 8.

Please replace the 3rd paragraph, lines 17-23, page 23, with the following:

pEGFP-C1 (GFP) and pEGFP-human Nox1 (GFP-Nox1) were separately transfected into the K-Ras-NRK/RNAi(1)-7 and K-Ras-NRK/RNAi(5)-7 by the same approach as in Example 4, then immunoblotting was conducted by the same approach as in Example 6 (Fig. 9). As shown in Example 6 and ~~the right panel of Fig. 7~~ in the left

panel of Fig. 8, neither RNAi(1) nor RNAi(5) inhibits human Nox1 expression. Therefore, even if the pEGFP-human Nox1 is transfected into the K-Ras-NRK/RNAi(1)-7 and K-Ras-NRK/RNAi(5)-7 cells, this human Nox1 is not inhibited by siRNA.

IN THE DRAWINGS:

Replace Fig. 12 with the amended Fig. 12 set forth in the "Replacement Sheet" attached hereto. The change in Fig. 12 is the addition of "Colony Counts" to the vertical axis.